

## REMARKS

### I. Support for the Amendments

Support for the amendment to the specification can be found in the application as filed, e.g., in the Transmittal Letter to the United States Designated/Elected Office (DO/EO/US) Concerning a Filing Under 35 U.S.C. 371 (priority date claimed 17 November 1998); in WO 00/29563 (published 25 May 2000) (copy included when application filed) (priority data listing U.K. application 9825215.8, filed 17 November 1998); and Notification Concerning Submission or Transmittal of Priority Document (PCT/IB/304; priority document received 6 December 1999) (copy included when application filed).

Support for claims 1, 3, 13, 14, and 25 as amended and for new claims 45-47 can be found in the original specification, e.g., from pages 2-5, in the Examples and in the original and amended claims. Detailed support for amended claims 1, 3, 13, 14, and 25 and new claims 45-47 can be found on pages 2-4, 5, and 6-7 of the specification, particularly in the carry-over paragraph on pages 2-3 and in claim 2 (now canceled), as well as in the middle paragraph on page 5. Claim 3 was previously dependent on claim 2. Claim 2 was canceled, and its limitations have been introduced into claim 1. Claim 3 has been amended to be dependent on claim 1. The language of claims 45-47 reflects the language of claims 25-27 prior to the present amendment, and additional support may be found in claims 25-27 as originally filed, in the carry-over paragraph on pages 2-3, and in the middle paragraph on page 5.

### II. Status of the Claims

Claims 1-35 and 37-44 were previously pending in the present application. In the Office Action, mailed 17 November 2003, the Examiner rejected claims 1-24, 28-35, and 37-44 and objected to claims 25-27.

Currently, claims 1, 3-35 and 37-48 are pending in the application, with claims 1, 13, 14, 24, 25, 30, 31, 34, 35, 37, and 48 being the independent claims. Claims 45-47 are new claims. Claim 2 has been cancelled without prejudice.

### **III. Acknowledgement of Receipt of Certified Copies of Priority Documents and Acknowledgement of Information Disclosure Statements**

In the Office Action Summary, the Examiner has acknowledged receipt of all certified copies of foreign priority documents from the International Bureau. The Examiner has also initialed the PTO-1449 Forms submitted on August 26, 2002, and on August 13, 2003.

Applicants wish to thank the Examiner for acknowledging the receipt of the priority documents and for initialing the PCT-1449 Forms.

### **IV. Assertion of the Priority Claim**

With respect to the priority claim, the Examiner noted:

The instant application is a 371 of PCT/GB99/03830, which appears to claim priority to a foreign document 9825215.8. Receipt is acknowledged of papers filed on November 17, 1999 purporting to comply with the requirements of 35 U.S.C. 119(a)-(d) and they have been placed of record in the file. Attention is directed to the fact that the date for which foreign priority is claimed is not the date of the first filed foreign application acknowledged in the oath or declaration.

If applicant desires priority under 35 U.S.C. 371 based upon a previously filed application, specific reference to the earlier filed application must be made in the instant application.... (Page 2.)

Applicants have amended the specification accordingly to include the "Cross-References to Related Applications" outlining the relationship of the present national stage

application (35 U.S.C. §371) to PCT/GB99/03830 (filed 17 November 1999; published as WO 00/29563 on 25 May 2000) and to U.K. application 9825215.8 (filed 17 November 1998), to which the PCT application claimed priority. Support for this amendment may be found on the cover page of the international publication WO 00/29563 and in the PCT Request (Form PCT/RO/101), copies of which are enclosed for the Examiner's convenience.

Furthermore, a certified copy of the U.K. priority application 9825215.8 was received by the International Bureau on 6 December 1999, as noted on the Form PCT/IB/304 (mailed 14 December 1999), which was enclosed with the application as filed. A copy of this form is enclosed for the Examiner's convenience.

In addition to the above copies, a copy of the Transmittal Letter to the United States Designated/Elected Office (DO/EO/US) Concerning a Filing Under 35 U.S.C. 371 is also enclosed. The priority claim was also acknowledged on the present Office Action Summary form.

The Examiner has further stated:

If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. **If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii).** This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c)....  
(Pages 3-4; emphasis in original.)

The basis for the priority claim has been established, *supra*.

Applicants wish to thank the Examiner for the time spent discussing this matter (especially in the telephonic interview of 17 February 2004), particularly with respect to 37 C.F.R. 1.55(a)(1)(ii) and (c), 35 U.S.C. §119(a)-(d), 35 U.S.C. §363, MPEP §204.14 and MPEP §204.14(a), especially the comments in the second paragraph following the quotation of 37 C.F.R. 1.55(c) in MPEP §204.14(a):

For nonprovisional applications **filed prior to November 29, 2000** and for design applications, a **claim for foreign priority may be made up until the time when the patent is granted....** (MPEP §201.14(a); emphasis added.)

As noted in 35 U.S.C. §363:

**An international application designating the United States shall have the effect, from its international filing date under article 11 of the treaty, of a national application for patent regularly filed in the Patent and Trademark Office** except as otherwise provided in section 102(e) of this title. (35 U.S.C. §363; emphasis added.)

Regardless of the date for the commencement of national phase, the present application has **an international filing date of 17 November 1999, which is prior to 29 November 2000**. Therefore, Applicants respectfully submit that a claim for foreign priority may be made up until the time when the patent is granted, as a matter of right.

The Examiner has since confirmed, during a subsequent telephonic interview, that Applicants may make the priority claim without the need to file a petition.

Applicants again thank the Examiner for her time and hereby request the Examiner to amend the specification accordingly.

**V. Rejection of Claims 1-12 under 35 U.S.C. § 112, Second Paragraph, Is Traversed**

The Examiner has rejected claims 1-12 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. In particular, the Examiner alleges:

Claims 1-12 are vague and indefinite in that the metes and bounds of the word "substantially" are unclear. The term "substantial" is a relative one not defined by the claim, no single set of conditions is recognized by the art as being "substantial" and because the specification does not provide a standard for ascertaining the requisite degree. (Page 4.)

Applicants respectfully disagree with this rejection.

First, the term "substantially" in the claims should not necessarily result in a rejection under 35 U.S.C. § 112. For example, the term "substantially" appears in the claims of numerous granted U.S. patents.

Second, according to Webster's Ninth New Collegiate Dictionary (1990), the word "substantial" is defined:

**sub-stan-tial**... **1 a** : consisting of or relating to substance **b** : not imaginary or illusory: REAL, TRUE **c** : IMPORTANT, ESSENTIAL **2** : ample to satisfy and nourish: FULL... **3 a** : possessed of means: WELL-TO-DO **b** : considerable in quantity: significantly large... **4** : firmly constructed: STURDY **5** : being largely but not wholly that which is specified.... (p. 1176; bold in original; underline added.)

A copy of this entry is enclosed for the Examiner's convenience.

Third, although the term "substantially" is not expressly defined in the specification, support for the use of a word such as "substantially" or the like, may be inferred from the description of the results of Example 1, as shown on page 6 in the Table of Extraction Mixtures Tested.

Claim 1 describes, in pertinent part, a method of "...forming an aqueous phase and a butanol phase,... wherein the genomic DNA is substantially in the aqueous phase and the plasmid DNA is substantially in the butanol phase..."

According to the description of the method of isolating plasmid DNA from a mixture of plasmid DNA and genomic DNA in Example 1, there are two phases: an aqueous phase and an organic phase (see top of page 6). The organic phase (e.g., a butanol phase) of each sample was removed and the plasmid DNA was precipitated (page 6). After a series of washes and resuspension, the "resultant plasmid-containing DNA solution could then be assayed by visualisation on an agarose gel and the amount of DNA determined quantitatively by spectrophotometry or by fluorescence." The Table of Extraction Mixtures Tested (pages 6-7) describes the Plasmid DNA Recovery as No, Poor, OK, or Good. "Good" is defined as "Approximately 1 µg DNA recovery"; "OK" is defined as "Approximately 200 ng DNA recovery"; and "Poor" is defined as "Just visible on agarose gel electrophoresis."

Clearly, some separation conditions are better than others. Those that are "OK," for example, have only some plasmid recovery. Therefore, it appears that, while these conditions are "OK" and, therefore, may be of some use, they do not result in an absolute sequestration of the plasmid DNA in the organic (e.g., butanol) phase. Rather, it may be that a larger percentage of the plasmid DNA in these samples is remaining in the aqueous phase with the genomic DNA. An "OK" plasmid recovery may be acceptable in some circumstances, even though only approximately 200 ng plasmid DNA, rather than approximately 1 µg plasmid DNA, is recovered (i.e., only 20% of the amount of DNA from a "Good" recovery).

Moreover, it is well-known to those of ordinary skill in the art that the difference between plasmid DNA and genomic DNA is readily observable on an agarose gel electrophoresis, due to the generally different sizes, conformations, and charges and, therefore, migration rates of the two types of DNA. The results of an agarose gel

electrophoresis, which not involve undue experimentation, would enable the practitioner of the present invention to observe whether the plasmid DNA was “substantially” in one fraction, while the genomic DNA was “substantially” in the other fraction.

For these reasons, Applicants respectfully traverse the Examiner’s rejection of claims 1-12 under 35 U.S.C. § 112, second paragraph, and assert that claims 1-12 are in a condition for allowance.

Therefore, Applicants request reconsideration and withdrawal of the rejections made under 35 U.S.C. §112, second paragraph.

**VI. Rejection of Claims 1, 4-6, 10-24, 28-35, and 37-44 Under 35 U.S.C. §112, First Paragraph, Is Traversed, but Partially Accommodated**

The Examiner has rejected claims 1, 4-6, 10-24, 28-35, and 37-44 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement, alleging that the claims contain subject matter, which is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

In particular, the Examiner alleges:

Applicants claim a method for isolating plasmid DNA from genomic DNA "under conditions to denature genomic DNA".

The written description requirement for genus claims may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with known or disclosed correlations between function and structure, or by a combination of such characteristics sufficient to show that the applicant was in possession of the claimed genus. Applicants teach that the instantly claimed invention distinguishes itself from the prior art by minimizing steps required for the

isolation of plasmid DNA from genomic DNA by the exploitation of the differential solubility between the two under denaturing conditions. Following denaturation, in the presence of extraction mixture comprised of chaotrope, butanol and water, genomic DNA separates into aqueous phases and plasmid DNA into butanol phase. Therefore, as an essential element, the invention claims a "condition" in which genomic DNA is denatured and can be retained in the aqueous phase of the extraction mixture and plasmid DNA selectively migrates into the butanol phase. In the instant specification, we are only taught that appropriate conditions for denaturation are high temperature of 65°C or higher for several minutes or basic conditions in which base is present as a hydroxide in concentrations of 100 mM to 200 mM (page 3, line 2-16). In the examples, sodium hydroxide in the range of 90 mM and 200 mM concentrations is alone exemplified and is shown to be adequate for "good" plasmid recovery (page 6-7, table). The disclosure of the afore stated conditions is not accompanied by a disclosure as to the relative properties of the condition that denatures DNA for retention in aqueous phases and yet allows plasmid DNA to migrate into the butanol phase. Therefore, there is no actual reduction to practice or clear description of what is required for "conditions to denature genomic DNA" to meet the limitations of the instant invention. Given **the diversity of conditions that denature DNA** and the inability to determine which will also meet the limitations of the instant invention, it is concluded that the invention must be empirically determined. **In an unpredictable art**, the disclosure of two species would not represent to the skilled artisan a representative number of species sufficient to show applicants were in possession of claimed genus. (Pages 4-6; emphasis added.)

Applicants respectfully disagree.

On pages 2-3, the specification provides:

In extraction step (i), the DNA-containing material is mixed with the reagents under conditions to denature the genomic DNA typically whereby the plasmid DNA is partitioned into an organic phase and the genomic DNA is partitioned into an aqueous phase. Such conditions include basic conditions or elevated temperature. Suitable elevated temperatures are of at least 65°C and more preferably in the range 70 to 95°C for a time sufficient to denature the plasmid DNA such as from about 30s to about 10mins, preferably around five minutes. Incubation times longer than about 10 minutes at elevated temperature should not adversely affect the plasmid DNA but are undesirable for using the organic solvent. In a preferred arrangement, basic conditions are used in which a base is present. The base is typically a hydroxide such as an alkali metal hydroxide, preferably sodium hydroxide. The base is preferably present at a concentration in the range 100mM to 200mM. Incubation time is usually in the range from about 30s to about 10 mins, preferably around five minutes. Excessive incubation under basic conditions can damage the plasmid DNA. (Pages 2-3.)



Applicants respectfully submit that this paragraph provides a wide range of conditions for the denaturation of genomic DNA. In addition, other conditions for denaturing DNA are known to those of ordinary skill in the art and would not necessarily require undue experimentation. Generally, Applicants need not be limited only to those conditions for which working examples have been provided (Examples 1 and 2). Reduction to practice is not required for every possible embodiment.

Moreover, it is not entirely clear what the Examiner regards as the “unpredictable art,” given “the diversity of conditions that denature DNA.” Conditions for denaturing DNA have been well known in the art for many years and have been used in a variety of applications, such as in dideoxy sequencing, library screening, and PCR.

Solely for the sake of furthering prosecution, however, Applicants have amended claims 1, 13, and 14 to include the limitations of claim 2. Claims 4-6, 15-23, and 38-44 are either dependent on claim 1 or on claims dependent on claim 1.

Claims 24, 30, 31, 34, and 35 provide extraction mixtures, rather than methods. The extraction mixtures may be used in the practice of the methods provided by the invention, which may comprise denaturation of the genomic DNA at a temperature of at least 65°C, which does not necessarily affect the composition of the extraction mixtures. Therefore, Applicants have not amended claims 24, 30, 31, 34, or 35. Claims 28, 29, 32, and 33 are dependent on claim 24, and the same arguments apply to these claims as well.

For these reasons, while Applicants respectfully traverse the Examiner’s rejection of claims 1, 4-6, 10-24, 28-35, and 37-44 under 35 U.S.C. § 112, first paragraph, Applicants respectfully assert that the amendments to claims 1, 13, 14, and 37 place claims 1, 4-6, 10-24, 28-35, and 37-44 in a condition for allowance.

Therefore, Applicants request reconsideration and withdrawal of the rejections made under 35 U.S.C. §112, first paragraph.

**VII. Objection to Claims 25-27 Is Accommodated and Rendered Moot to Place Claims 25-27 in Condition for Allowance**

The Examiner has objected to claims 25-27 as being dependent upon a rejected base claim (page 6), but has indicated that these claims “would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.”

Applicants have amended claim 25 to accommodate the Examiner’s suggestions. Claims 26 and 27 are dependent on claim 25 or on a claim dependent on claim 25. Applicants respectfully submit that these claims are now in a condition for allowance and request the Examiner to allow these claims accordingly.

### VIII. Conclusion

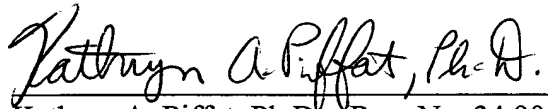
It is believed that all outstanding rejections have been addressed by this submission and that all the claims are in condition for allowance. If discussion of any amendment or remark made herein would advance this important case to allowance, the Examiner is invited to call the undersigned as soon as convenient.

In view of the foregoing amendments and remarks, the present application is respectfully considered in condition for allowance. An early reconsideration and notice of allowance are earnestly solicited.

Applicants hereby request a two-month extension of time for the Amendment and accompanying materials. Although it is not believed that any additional fee (in addition to the fee concurrently submitted) is required to consider this submission, the Commissioner is hereby authorized to charge our deposit account no. 04-1105 should any fee be deemed necessary.

Respectfully submitted,

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